Diagnosis and Non-Surgical Management of Mesenteric Ischemia

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Introduction
Mesenteric ischemia is an uncommon but serious disease. It was reported by Conner in 1933, who postulated that patients with chronic abdominal pain may have actually suffered from repeated intestinal angina.1 Mesenteric ischemia can be either acute or chronic. Acute mesenteric ischemia (AMI) is further subdivided into occlusive and nonocclusive mesenteric ischemia. Oclusive mesenteric ischemia is thrombotic or embolic in origin. Approximately 80% of cases of AMI are occlusive in etiology, with arterial emboli or thromboses in 65% of the cases. Nonocclusive mesenteric ischemia is due to arterial hypoperfusion, most commonly a result of primary splanchic vasoconstriction and low-flow states. Chronic mesenteric ischemia (CMI) refers to episodic or constant intestinal hypoperfusion, which usually develops in patients with atherosclerotic vascular disease. CMI is being diagnosed in an increasing number of individuals, possibly the result of an aging population. We briefly describe a patient with mesenteric ischemia and further discuss the diagnosis and endovascular management options.

Case
An 83-year-old, African-American female with a history of type 2 diabetes mellitus type, hypertension, gastroesophageal reflux disease and hyperthyroidism presented with post-prandial abdominal pain for approximately three months. The pain was dull and achy in character, which predominantly started in the epigastric region radiating to her left shoulder. She had significant weight loss of about 50 pounds, anorexia over the past 8 months and nausea for about 3 to 4 months. She did not experience significant vomiting or constipation. However, she complained of increased flatulence. She had no previous history of hepatitis, pancreatitis, or gastric or duodenal ulcers. There was no known history of cholelithiasis or cholecystitis. The patient also complained of increased peristalsis soon after she eats, with occasional diarrhea. She worked all her life as a farmer, denied smoking or drinking alcohol, however, dips snuff. She had never traveled outside the United States and denied any exposure to tuberculosis.

On physical examination, her vital signs were stable. Her temperature was 36.8, blood pressure was 140/60, regular heart rate was 84, and respiratory rate was 18. She was thin and cachectic-looking, with no obvious distress. There was no scleral icterus noted. Her cardiac examination revealed a regular rhythm with a 2/6 ejection systolic murmur heard at the murmur left sternal border. Her lungs were clear to auscultation. Her abdomen was soft, non-distended with no mass palpated. She had mild tenderness at her epigastric region with no guarding, rigidity or rebound. She had normal bowel sounds in all four quadrants with no bruits. Blood work showed a hemoglobin of 9.0 g/dl and hematocrit of 27. Her white blood cell count (WBC) and platelets were within normal range. Her metabolic panel showed sodium to be 136 mEq/l, potassium 2.8 mEq/l, chloride 99 mEq/l, and HCO3 27 mEq/l. Her renal function was normal. Her liver panel showed albumin 2.9 g/dl, total bilirubin 0.6 mg/dl, direct bilirubin 0.2 mg/dl, SGOT 16 U/L, SGPT 4 U/L, alkaline phosphatase 77 U/L. Her serum amylase and lipase levels were elevated in the range of 689 U/L and 668 U/L, respectively.

She underwent an acute abdominal series that was non-diagnostic with heavy vascular calcification, and non-specific bowel gas pattern. Gas was visualized in the colon. There were no dilated loops seen to suggest obstruction. Because of the clinical presentation and elevated amylase and lipase, the patient was admitted to the hospital with a diagnosis of pancreatitis for further management. The patient underwent a computed tomography (CT) of her abdomen. Contiguous axial images of the abdomen and pelvis were obtained after administration of intravenous and oral contrast. It showed severe atherosclerotic disease of the abdominal aorta and the origin of the superior mesenteric artery (SMA) appeared to be severely stenotic and possibly occluded proximally. The distal branches of the superior mesenteric artery appeared to be patent. Computed tomographic angiography (CTA) was done the following day to further evaluate the abdominal aorta and mesenteric arteries. CTA showed a 2 cm segmental occlusion of the proximal SMA with calcific plaque at the ostium. The distal SMA was reconstructed by way of inferior mesenteric artery (IMA) collaterals. The IMA was a
large artery with an ostial stenosis estimated at 70%. Subtotal occlusion of the celiac artery (CA) at the ostium was also identified.

Mesenteric angina was diagnosed and with persisting abdominal pain, the patient underwent a mesenteric angiogram, which confirmed the findings of the CTA. The patient underwent a successful angioplasty and stenting of the SMA. Her proximal lesion was initially dilated with a 2.5 mm x 30 mm Voyager balloon (Guidant Corp., Santa Clara, California), followed by a 4.0 mm x 30 mm Aviator balloon (Cordis Corporation, Miami, Florida). Due to suboptimal results of the balloon angioplasty, a 5.0 mm x 18 mm Genesis stent (Cordis) was placed in the ostial and proximal portion of the SMA. Post procedure pictures showed good flow into SMA with less than 10% residual stenosis. The patient was able to tolerate oral intake well without any abdominal pain, and her amylase and lipase levels normalized. She was discharged home under stable conditions and is being followed up as an outpatient.

**Pathophysiology**

The most important factor that determines the severity of chronic mesenteric ischemia (CMI) is blood flow. Intestines receive blood supply from extensive collateral circulation from the celiac axis, superior and inferior mesenteric arteries. This extensive collateral circulation and the intrinsic autoregulation of blood flow by the splanchnic vessels is thought to occur in response to acute reductions in perfusion pressure, protecting the intestines from transient periods of inadequate perfusion. Direct arteriolar smooth muscle relaxation and metabolic responses to adenosine and other metabolites of mucosal ischemia by the splanchnic blood vessels maintain adequate blood flow to the intestines even during wide variation in the cardiac output. However, prolonged reduction in splanchnic blood flow leads to vasoconstriction in the affected vascular bed, which eventually reduces the collateral blood flow.

Generally, at least two of these vessels must be compromised to produce symptomatic intestinal ischemia. The exceptions are inpatients who have had previous abdominal surgery and also in patients with median arcuate ligament syndrome. In patients with previous surgery, the collaterals may be interrupted, and hence they are prone to ischemia, even with a single vessel occlusion. Patients with celiac artery compression syndrome (also referred to as celiac axis syndrome, median arcuate ligament syndrome and Dunbar syndrome) have abdominal pain related to compression of the celiac artery by fibers of the median arcuate ligament even though the superior mesenteric artery (SMA) and the inferior mesenteric artery are widely patent. Various intrinsic factors, including the competence of systemic perfusion, collateral circulation, the number and caliber of splanchnic vessels that are affected, and the duration
of the ischemic insult, determine the likelihood of developing intestinal ischemia. These vessels are affected in patients with poor systemic circulation due to atherosclerosis, narrowing of the major mesenteric vessels, embolic events and vasculitis as seen in systemic diseases, which can result in poor blood flow in the mesenteric arteries, leading to ischemia.19

Mesenteric atherothrombosis also predominantly affects the SMA, with proximal SMA the most commonly affected area. Hence, the proximal jejunum through the distal transverse colon becomes ischemic. It is seen in patients with severe atherosclerosis. Patients have a history of abdominal pain after meals (post prandial) with associated weight loss secondary to poor oral intake.7 This is seen in about 20–50% of patients with SMA thrombosis. These patients are often elderly, with coronary artery disease (CAD), severe peripheral vascular disease (PVD) and hypertension. SMA thrombosis presents with gradual onset of abdominal pain and distension. A history of post-prandial abdominal pain and weight loss is present in half of cases. In patients with acute mesenteric ischemia, the pain is usually out of proportion to the physical findings, and nausea and vomiting are common. Other signs of PVD, such as carotid, femoral or abdominal bruits, or decreased peripheral pulses, are frequently seen. As the occlusion gets severe, abdominal distension, absent bowel sounds, guarding, rebound and localized tenderness, and rigidity start developing.

The major causes of acute mesenteric ischemia are embolism or thrombosis of the SMA. Thrombotic lesions are usually seen at the origin or the proximal portion of the vessel, while the emboli are usually seen in the distal portion. Mesenteric arterial embolism should be highly suspected in patients around the age of 70 years who present with acute onset of abdominal pain. The majority of emboli lodge in the SMA. Less frequently, celiac or IMA embolization can also lead to acute ischemia. Various systemic risk factors predispose the development of mesenteric emboli. Emboli originating from the left atrium or ventricle are the most common cause of SMA embolism. Other risk factors include advanced age, CAD, valvular heart disease, cardiac dysrhythmias, atrial fibrillation, post-myocardial infarction (MI) mural thrombosis, and history of thromboembolic events, aortic surgery, aortography, coronary angiography, hypercoagulable states and aortic dissection.

Mesenteric vein thrombosis can also cause acute ischemia.19 In patients who present with mesenteric venous thrombosis, 75% have either an inherited or acquired thrombotic disorder.11 The most commonly acquired thrombotic disorder seen in patients with mesenteric ischemia is the factor V Leiden mutation, causing resistance to activated protein C, and commonly acquired hypercoagulable states are paroxysmal nocturnal hemoglobinuria and the myeloproliferative syndromes.12

Nonocclusive mesenteric ischemia (NOMI) is seen as a result of splanchnic hypoperfusion and vasoconstriction is seen predominantly in elderly patients with significant atherosclerotic vascular disease13 in the setting of low-flow states. It is commonly seen after a life-threatening complication (acute MI or congestive heart failure) or post cardiac surgery, in patients who are also being treated with drugs known to reduce intestinal perfusion (such as diuretics).14 It can also be seen in patients with aortic insufficiency, sepsis, cardiac arrhythmias and in patients who are receiving medications such as alpha-adrenergic agonists.15 Several cases of NOMI resulting from cocaine use have also been described, particularly in young individuals.14 The pathogenesis of NOMI is related to vasopressin- and angiotensin-mediated mesenteric vasospasm, which functions to maintain cardiac and cerebral blood flow at the expense of the splanchnic and peripheral circulation.15 The villus tips are most susceptible to injury because of their relatively high oxygen requirement. Despite the decline in its incidence, NOMI results in a very high mortality of nearly 70%, due to the difficulty in making the diagnosis and reversing the ischemia once it has started, as well as the underlying hemodynamic state of the patient.16

Clinical Presentation

Diagnosis can be a challenge for clinicians because symptoms are frequently complex and can vary among patients. Approximately two-thirds of patients with AMI are women. The diagnosis of AMI depends upon a high index of clinical suspicion, especially in patients with risk factors. Patients usually present with a sudden onset of severe but poorly localized periumbilical pain, associated nausea, vomiting and frequent bowel movements. Pain is usually out of proportion to the physical findings, and sometimes may be the only presenting symptom. On physical examination, the abdomen is soft with only mild tenderness. Signs of peritoneal irritation, like rigidity and guarding, are often delayed and may take hours to develop. Absence of bowel sounds, abdominal distension or guarding is indicative of severe disease. Blood per rectum is present in about 16% of patients, and occult blood is present in 25% of patients. Patients start developing peritoneal signs when the ischemic process becomes transmural. Most laboratory abnormalities are found to be elevated only after the ischemic insult has progressed to bowel necrosis.17 WBC is elevated in most cases of mesenteric ischemia, ranging anywhere from 10-15,000/mm³ in 25%, 15–30,000 in 50%, and > 30,000 in about 25% of patients. Metabolic acidosis and elevated serum amylase levels can also be seen in patients with mesenteric ischemia. Lange et al. found that elevation in the serum lactate was 100% sensitive, but only 42% specific for intestinal ischemia/infarction.18 Elevated amylase levels have been seen in about 50% of patients with intestinal ischemia7 and phosphate elevation in 80% of
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patients. Creatinine kinase-BB isoenzyme elevations have also been noted to be elevated in these patients. Alpha-glutathione s-transferase (alpha-GST) and intestinal fatty acid-binding protein (I-FABP) are some new tests available that may help to diagnose mesenteric ischemia. An elevated alpha-GST has a 72% sensitivity and 77% specificity for diagnosing AMI. However, it can not help distinguish between ischemia and infarction. Alpha-GST has a negative predictive value of 90% when combined with serum lactate, and 100% when combined with the normal WBC.

Radio logical Diagnosis

Due to the vague, nonspecific clinical presentation and unreliable physical signs with mesenteric ischemia, radiographic studies play a very important role in the diagnosis and management of mesenteric ischemia. The noninvasive tests that are available include plain abdominal x-rays, Doppler ultrasonogram (US), computerized tomography (CT) and magnetic resonance imaging (MRI).

Plain abdominal x-ray findings are non-specific and abnormalities are usually seen only late in the course of the disease; however, they may show the presence of an ileus with distended loops bowel and bowel wall thickening. Wall thickening is usually seen with acute mesenteric venous thrombosis. With severe advanced ischemia, air in the bowel wall may be seen (pneumatosis intestinalis). Abdominal films may be completely normal in more than 25% of patients. Barium studies offer little additional information, and also interfere with visualization on angiography. The classic thumbprinting described with barium studies indicates submucosal hemorrhage or edema, resulting in focal mural thickening.

Postprandial Doppler flow changes in the mesenteric arteries are widely used to detect to inflammatory diseases like Crohn's disease, celiac disease and ulcerative colitis. It has not been found to be very helpful in the diagnosis of acute mesenteric ischemia. It may be able to visualize stenosis or occlusions in the celiac or superior mesenteric arteries. However, the test is often technically limited due to the presence of air-filled bowels, fluid and abdominal distension. It has also been shown to have poor sensitivity in low-flow disease. There is also significant inter- and intra-observer variability in echo-Doppler measurements of superior mesenteric artery blood flow. Because of these drawbacks, and the excess time required to attempt duplex scanning, the recent guidelines by the American College of Cardiology, American Heart Association, and Society for Vascular Medicine and Biology have not recommended the test in AMI.

CT and MRI of the abdomen have replaced plain films and ultrasound in the diagnosis of mesenteric ischemia. These are the most sensitive noninvasive diagnostic tests and should be obtained early, particularly for any patient suspected of mesenteric vein thrombosis. CT shows focal or segmental bowel wall thickening, submucosal edema or hemorrhage, and intestinal pneumatosis with portal vein gas. Timed contrast sequences will show mesenteric venous occlusions by the lack of enhancement of the arterial vasculature. In a study by Taourel et al., intramural gas, portal venous gas, focal lack of bowel-wall enhancement, liver or splenic infarcts had a sensitivity and specificity of 64% and 92%, respectively, to diagnose mesenteric arterial or venous thrombosis. The presence of pneumatosis intestinalis on CT, however, does not necessarily indicate transmural infarction. Patients with transmural infarction have pneumatosis with portomesenteric venous gas.

Recent developments in magnetic resonance angiography (MRA) and multidetector row CT (MDCT) can provide detailed information about the mesenteric vessels and the small bowel. Excellent visualization of the vascular anatomy, in addition to assessment of portal venous patency, flow direction, splanchnic thrombosis and changes suggestive of portal hypertension, is possible with MRI. However, it is as yet unclear whether these studies can accurately detect the presence of small thromboemboli, early reversible ischemia or non-occlusive ischemia due to low-flow states or distal emboli. Though initial experiences suggest MRA to be highly sensitive for the diagnosis of mesenteric venous thrombosis, CT is still preferred because of its lower costs, wide availability, and excellent sensitivity for diagnosing SMV thrombosis. The advantage of MRI is the use of safer gadolinium agents and lack of ionizing radiation.

Angiography remains the gold standard for diagnosing acute arterial ischemia. It is essential to obtain various views to completely evaluate the mesenteric and celiac territories. The lateral view outlines the origins of the celiac axis and SMA, while the distal celiac axis and remainder of the SMA are best seen in the anteroposterior projections. Angiography is, however, relatively less sensitive for superior mesenteric vein thrombosis. Angiography is still recommended if there is a clinical suspicion of small thromboemboli that are not seen by CT or MRA. The decrease in threshold by the physicians to use angiography to diagnose mesenteric ischemia has played a major role in the decline in the mortality of patients with acute mesenteric ischemia over the past 30 years. The relative contraindications include renal insufficiency and hypotension or hypovolemia, because of the potential risk of increasing vasoconstriction, resulting in the decrease of the specificity.

Treatment

Early diagnosis and revascularization to prevent disease progression of ischemia to infarction, ameliorate pain and to prevent possible death from development of complications is key to the management of mesenteric ischemia.

Open surgery has been the mainstay of treatment for CMI. Patients with CMI usually have many comorbidities and significant perioperative risk. Weight loss and malnutrition significantly increases the risk of complications.
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During surgery and in the post-operative period, patients undergoing open revascularization have significant perioperative mortality and morbidity, including death, MI, acute renal failure, respiratory failure, mesenteric infarction or multiorgan dysfunction. Studies have shown perioperative complications during surgical interventions occurring in the range of 19–54% and mortality ranging from 0 to 17%. Recent reports have shown a technical success rate ranging from 92% to 100% for percutaneous stent placement for CMI, with perioperative mortality rates of 0% to 10%, and morbidity from 0% to 17%. Thus, percutaneous approaches to treat mesenteric and celiac stenosis have become an attractive option to patients and physicians. Recurrence of symptoms nearly always indicates recurrence of the arterial occlusion, requiring repeat intervention percutaneously or surgically.

The treatment options for AMI depend on the severity of the occlusion and the patient’s clinical condition. Patients without peritoneal signs with minor emboli, who achieve pain relief with vasodilator infusion, could be managed nonoperatively with repeated angiograms. In patients presenting with acute mesenteric ischemia secondary to thrombosis or a large embolus, treatment is started even while undergoing angiography with papaverine infusion. In non-occlusive mesenteric ischemia, infusion of the intra-arterial vasodilator papaverine may be all that is necessary to reverse vasoconstriction and prevent bowel infarction. Patients who have thrombi with good collateral vasculature and without peritoneal signs could also be treated conservatively with bowel rest and observation in the hospital, without a papaverine infusion. In the absence of peritoneal signs, though surgical embolectomy is considered the treatment of choice, percutaneous approach has been effectively used. Intra-arterial infusion with thrombolytic agents such as streptokinase, urokinase, or recombinant tissue plasminogen activator has been shown to be effective when used within 12 hours of the onset of symptoms. Patients with peritoneal signs and documented thrombosis with mesenteric ischemia, infarction, bowel ischemia and bowel infarction require laparotomy for possible thrombectomy and mesenteric revascularization, with aortomesenteric bypass grafting and resection of infarcted bowel. Occasionally, patients might need a “second look” operation 24 to 48 hours after the initial procedure to avoid potential risk of resection of excess viable bowel and failure to resect non-viable bowel. For all patients with mesenteric ischemia, long-term postoperative anticoagulation is recommended.

Endovascular Technique

A detailed explanation of the percutaneous techniques used in mesenteric ischemia is beyond the scope of our article. Diagnostic angiography is mandatory prior to intervention to help delineate the ostium of the mesenteric vessels. The presence of collaterals, especially the maneuvering mesenteric artery, arc of Riolan and artery of Drummond, should be identified. If two out of the three mesenteric vessels demonstrate a significant stenosis, revascularization of one mesenteric vessel is warranted. In some occasions, ostial compression by the diaphragm during respiration can mimic stenosis (median arcuate ligament syndrome). Selective mesenteric vessel angiography will delineate both ostial and lesions along the course of the vessels. Accessing the inferior mesenteric artery could be difficult; however, it seldom requires revascularization. Access to the mesenteric vessels can be accessed via the brachial artery or femoral artery, depending on the takeoff of the vessel in relation to the aorta. The femoral approach provides more support, while a down-sloping SMA is best approached with a brachial access. Ostial lesions are approached with a “no-touch technique” or “telescoping technique,” and selective cannulation of the mesenteric vessels with a 0.014” wire is desirable. Predilatation with a low-profile, semi-compliant balloon is recommended. In cases with sub-optimal results with balloon angioplasty (residual stenosis > 50% or a flow-limiting dissection), a balloon-expandable stent implantation for ostial and proximal lesions will result in adequate reperfusion. Mid to distal segments of the mesenteric vessels rarely develop stenosis. If encountered, they are best treated with balloon angioplasty and a self-expanding stent. We recommend a 1:1 sizing of the balloon/ stent to vessel diameter, while aggressive over-sizing of the balloon or stents should be avoided.

Conclusion

The clinical spectrum of mesenteric ischemia is quite extensive. Signs and symptoms of mesenteric ischemia can be nonspecific and a nightmare for the diagnosing physicians. The diagnosis depends upon a high index of suspicion, especially in patients with risk factors like atrial fibrillation, PVD, CHF and hypercoagulability. Chronic mesenteric ischemia should be considered as a differential diagnosis for all abdominal pain patients after other more common causes are excluded. Timely recognition is essential to prevent catastrophic outcomes due to intestinal infarction. The goal of the treatment is to restore blood supply to the intestines as early as possible. An aggressive approach, combining surgical and radiological expertise, is essential to decrease mortality and morbidity in these patients. With the advances made in percutaneous angioplasty and stenting, the physicians have one more tool in their armamentarium to successfully treat mesenteric ischemia.

References

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